Human Performance and Biosystems

March 2014

Spring Review

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Program Officer
AFOSR/RTE
Air Force Office of Scientific Research

Integrity ★ Service ★ Excellence

Human Performance and Biosystems Program

- **Investigates scientific challenges of Bioenergy from cells**
- **Develops a mechanistic understanding of microbes, nanowires and their energy transfer processes**
- **Studies electrical transfer capabilities between biotic and abiotic surfaces**

Air Force Relevance

Sensors: mapping of Brain/neural activity for cognitive enhancement

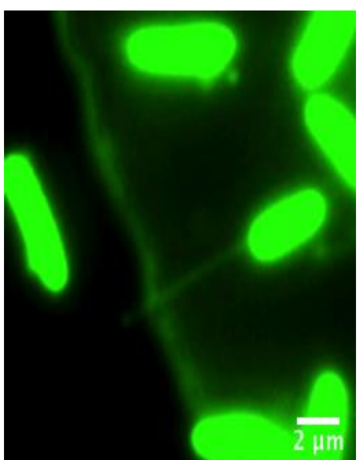
:Early detection of cell product and pathway processes

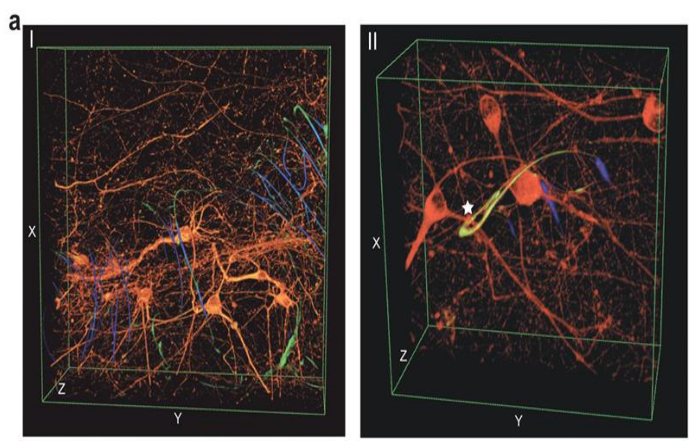
Areas of Emphasis

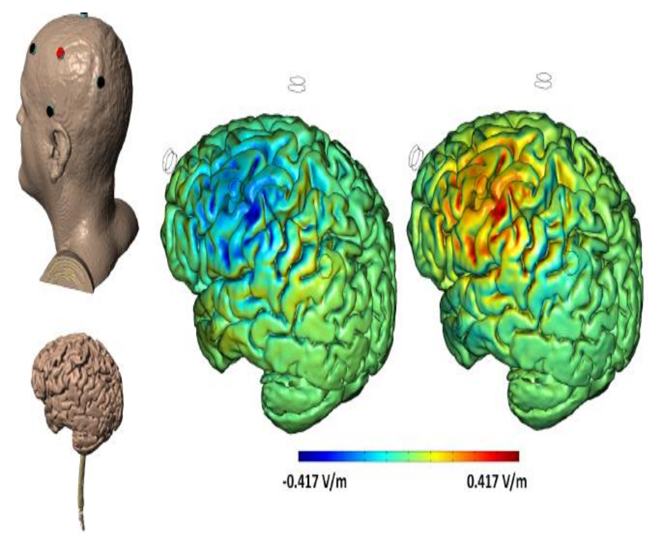
Biofilms/Nanowires – microbe communication, extracellular electron transfer, cyborg cell

Trans cranial direct current stimulation – neuronal pathways, biochemical/electrophysiological changes

Biomarkers – breath based, sweat based, odor based







Program Trends

- Enzymatic/Microbial Fuel Cells
- Artificial Photosynthesis
- Algal oil generation

- Biofilm, Nanowires,Cyborg Cell
- tDCS
- Biomarkers

Program Interactions

tDCS/Cyborg cell

Microbes/nanowires

Biomarkers

BRI magnetic navigation

Synthetic Biology

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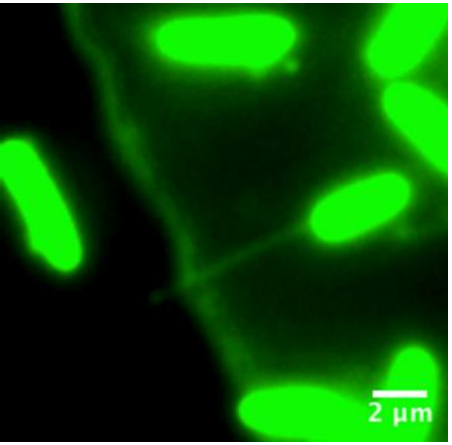
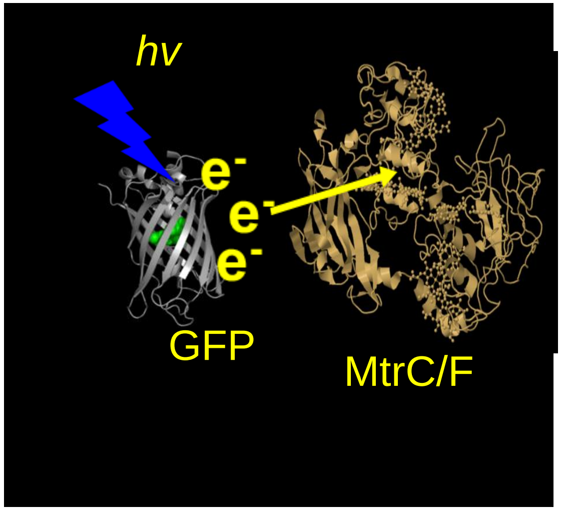
Biofilms and Nanowires Challenges



Channel electronic signals between synthetic devices and the electron transport chains of live cells

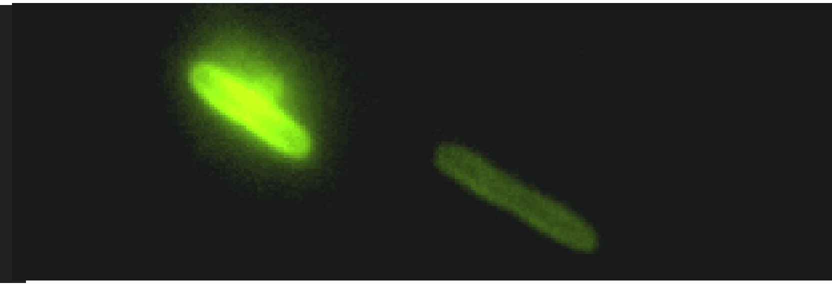
Develop solid-state and molecular (electrode-free) interfaces to bacterial nanowires, for control of cellular bioenergetics

Channel photo-excited states into donating electrons to multiheme cytochromes instead of fluorescence



Control of Electron Exchange via Bacterial Nanowires at Hybrid Living-Synthetic Interfaces
El-Naggar (USC)

Physiological switch: Developed methodology to physiologically induce bacterial nanowires in microfluidic devices as shown here by switching to extracellular respiration conditions.



Next-generation sequencing

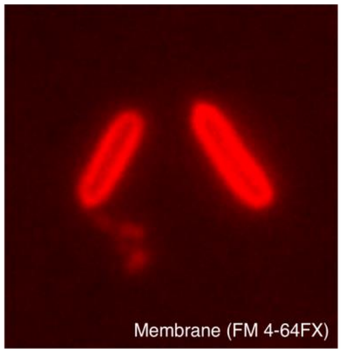
Synthetic interface to device via cell metabolic activity

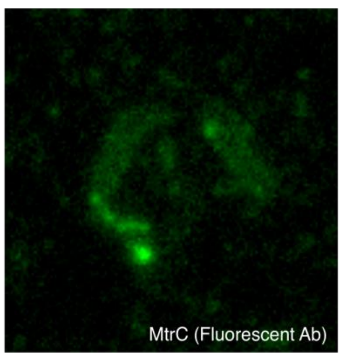
Can we achieve a genetic switch?
Long-term goal: Synthetic biology approach for transferring the extracellular electron transport function naturally existing in microbes to other cell types.

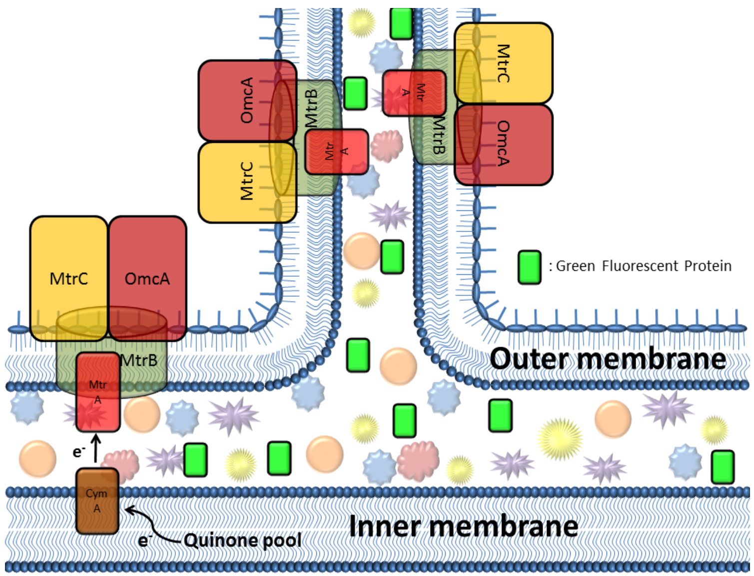
Can we "plug" cells directly to synthetic devices using this same methodology?
Long-term goal: Connecting and powering a synthetic device using cellular metabolic activity

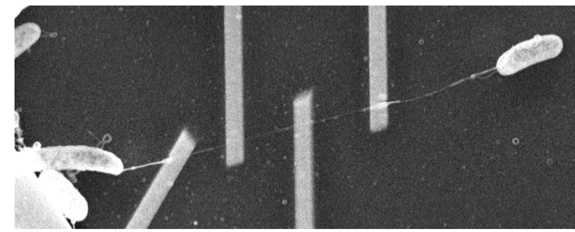
Extracellular Electron Transport: Bacterial Nanowires

Discover the **nanoscale** spatial organization of electron transport proteins in bacterial nanowires



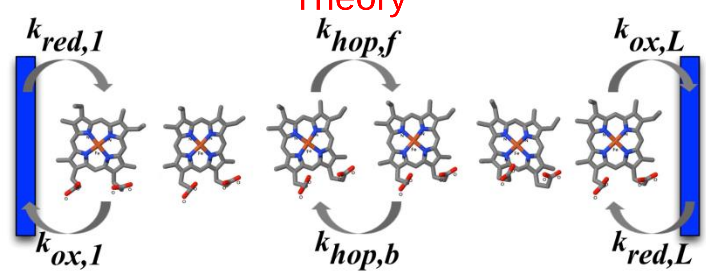






Experiment

Theory



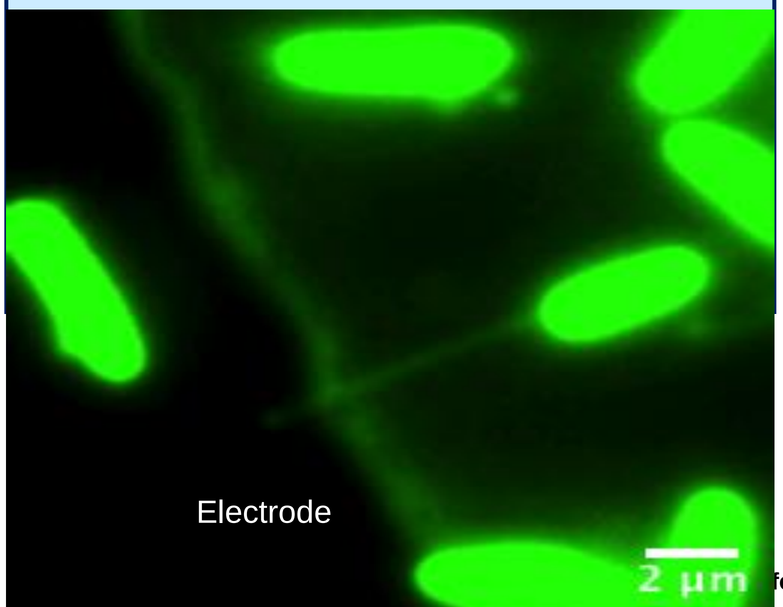
Goal - channel electronic signals between synthetic devices and the electron transport chains of live cells.

Interfacing to the Electron Transport Chain of Living Cells

Develop both **solid-state and molecular (electrode-free) interfaces to bacterial nanowires**, to control cell bioenergetics

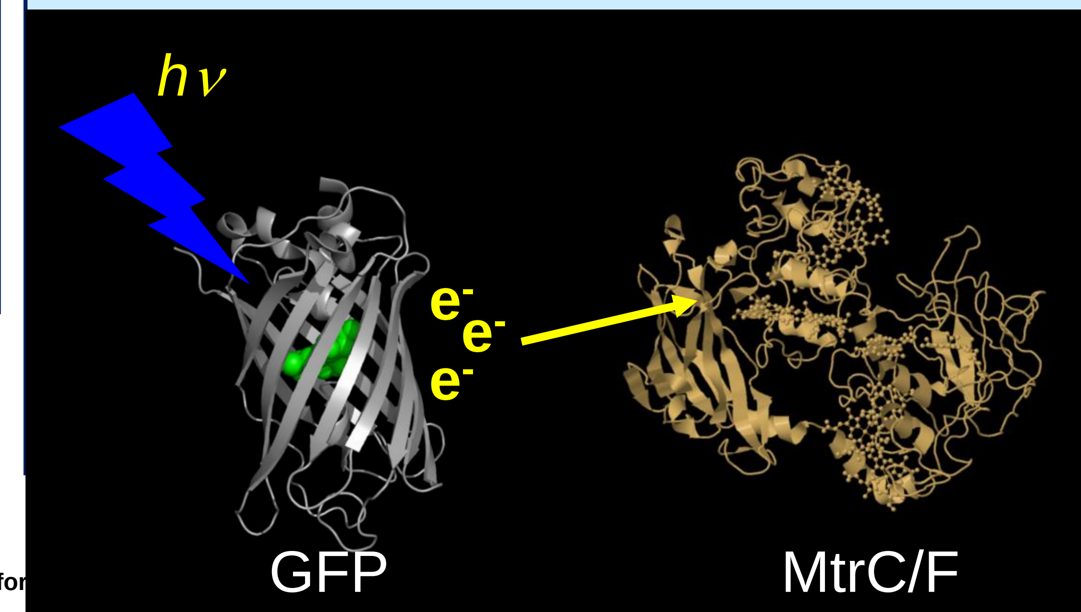
Solid-state interfaces:

Nanowires membrane = lipid-based. Does a phospholipid-coated metalloxide electrode increase connectivity?



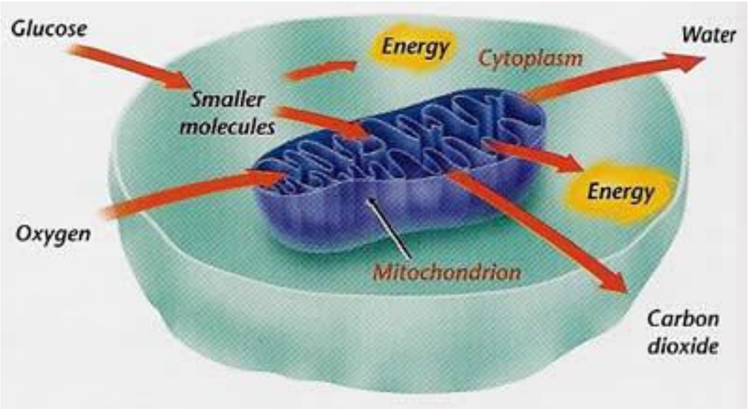
Molecular "Stealth" interfaces:

Basic idea: channel photo-excited states into donating electrons to multiheme cytochromes instead of fluorescence.

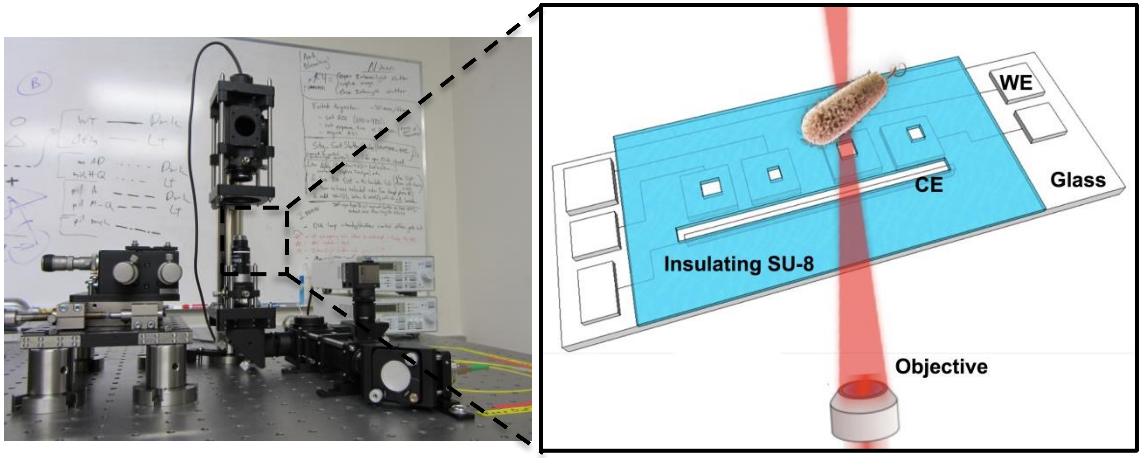


Transfer our Knowledge to Eukaryotic Cells: Mitochondrial Electron Transport

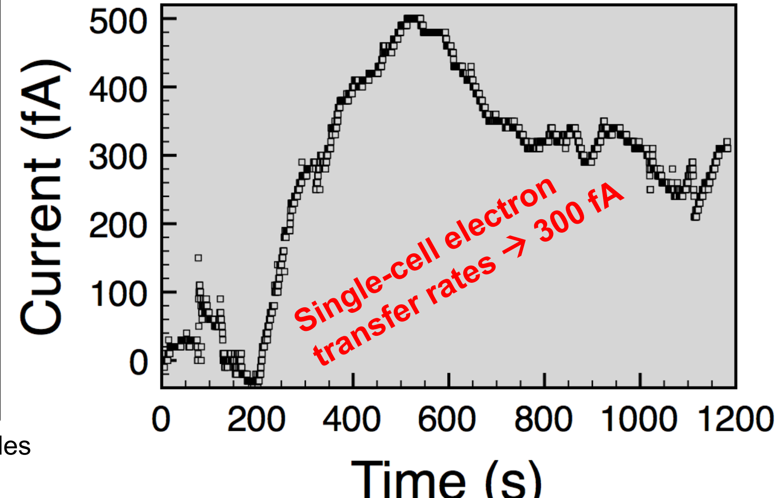
Can bacterial extracellular electron transport and bacterial nanowire functionality be relevant to mitochondria?



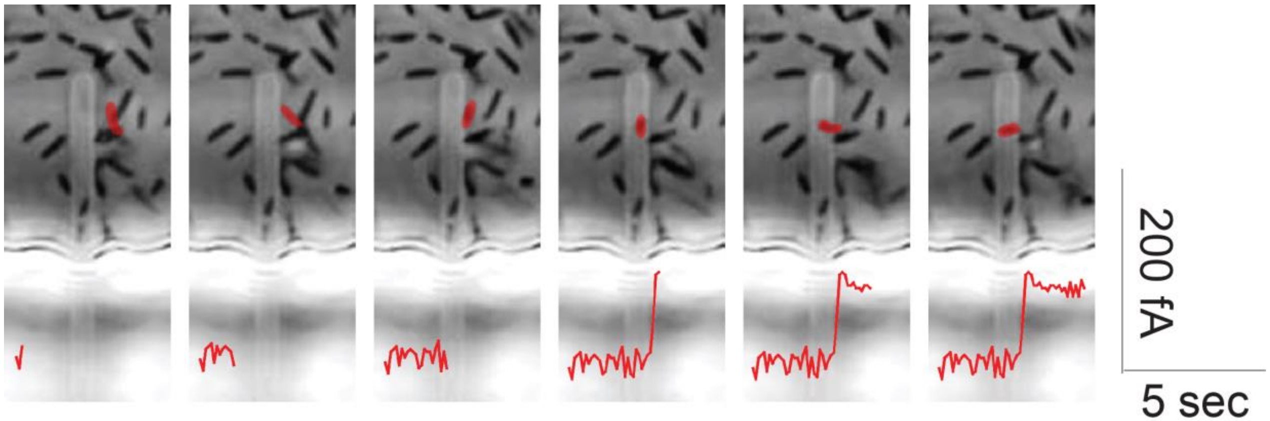
Adapt a technology developed for bacterial electron transport, while studying the feasibility of expressing bacterial ET components in mitochondria (high risk):

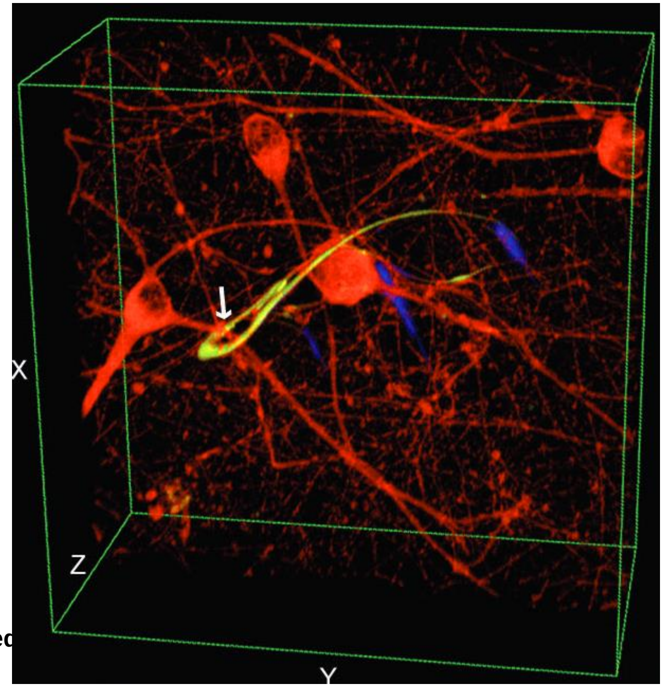


Manipulation and ET measurements of individual microbes on microscale "landing pad" electrodes



Nanoelectronic Structures for Single Cell to Cell-Network Interfaces – Cyborg Cell

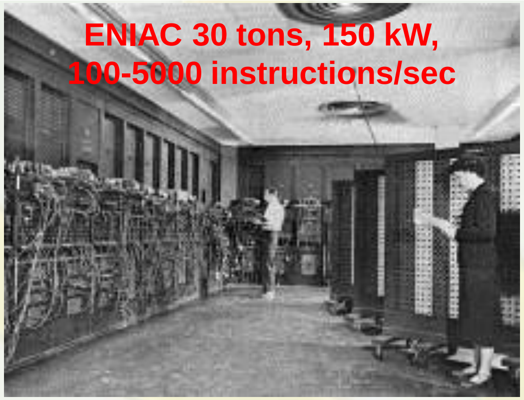


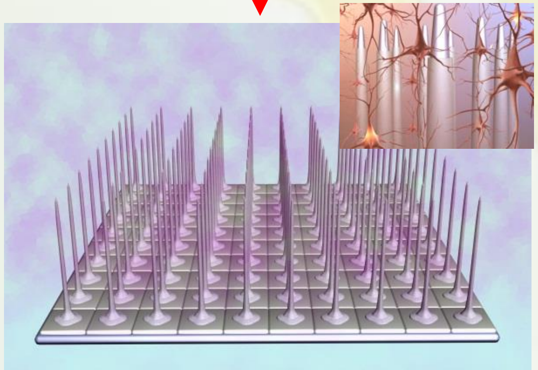


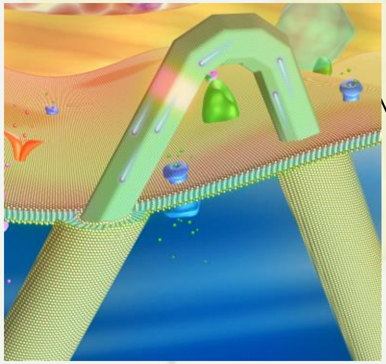
Charles M. Lieber

Harvard University

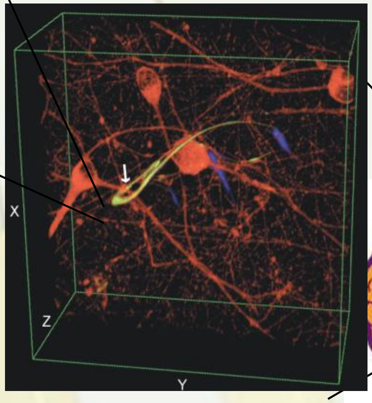
Future: Interfaces to Cells, Tissue & Organs

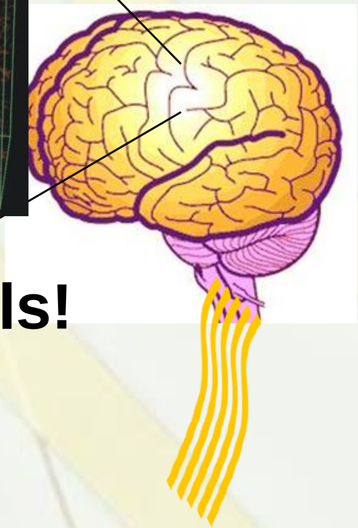






Novel Tools!





New Materials!

"Blur the distinction between electronic devices, circuits, living cells & tissue!"

Nanoelectronic Structures for Single Cell to Cell-Network Interfaces to "tissues" - Cyborg Cell

Challenges:

-Finding external energy source
-Determining how to manipulate and measure organelle changes
-How to deliver this to the system

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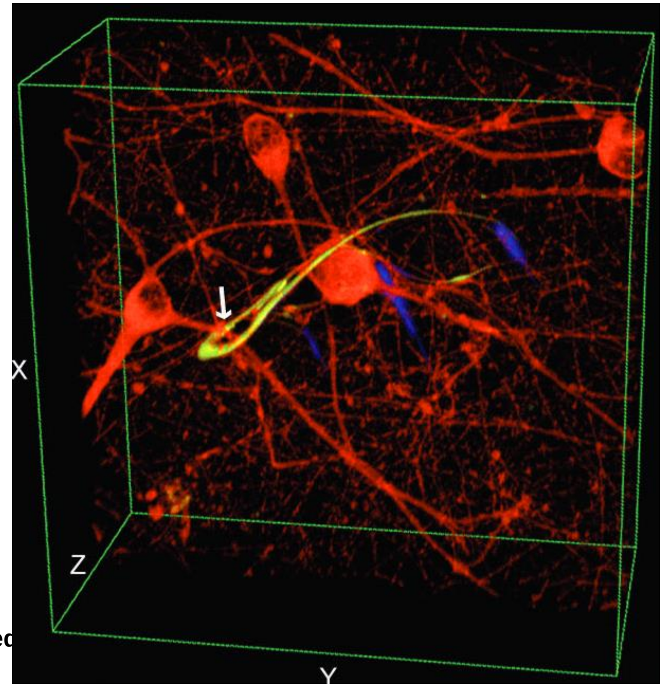
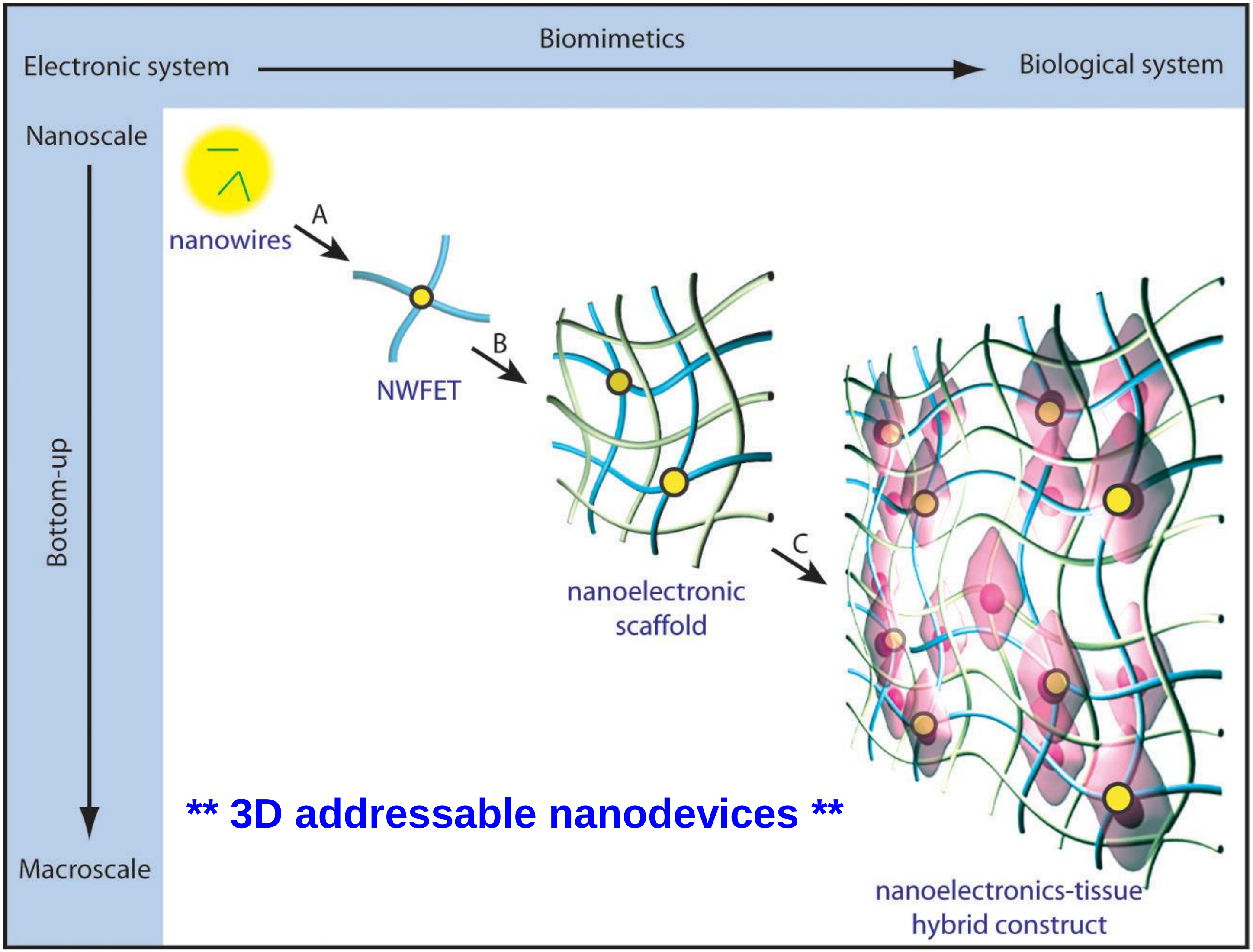
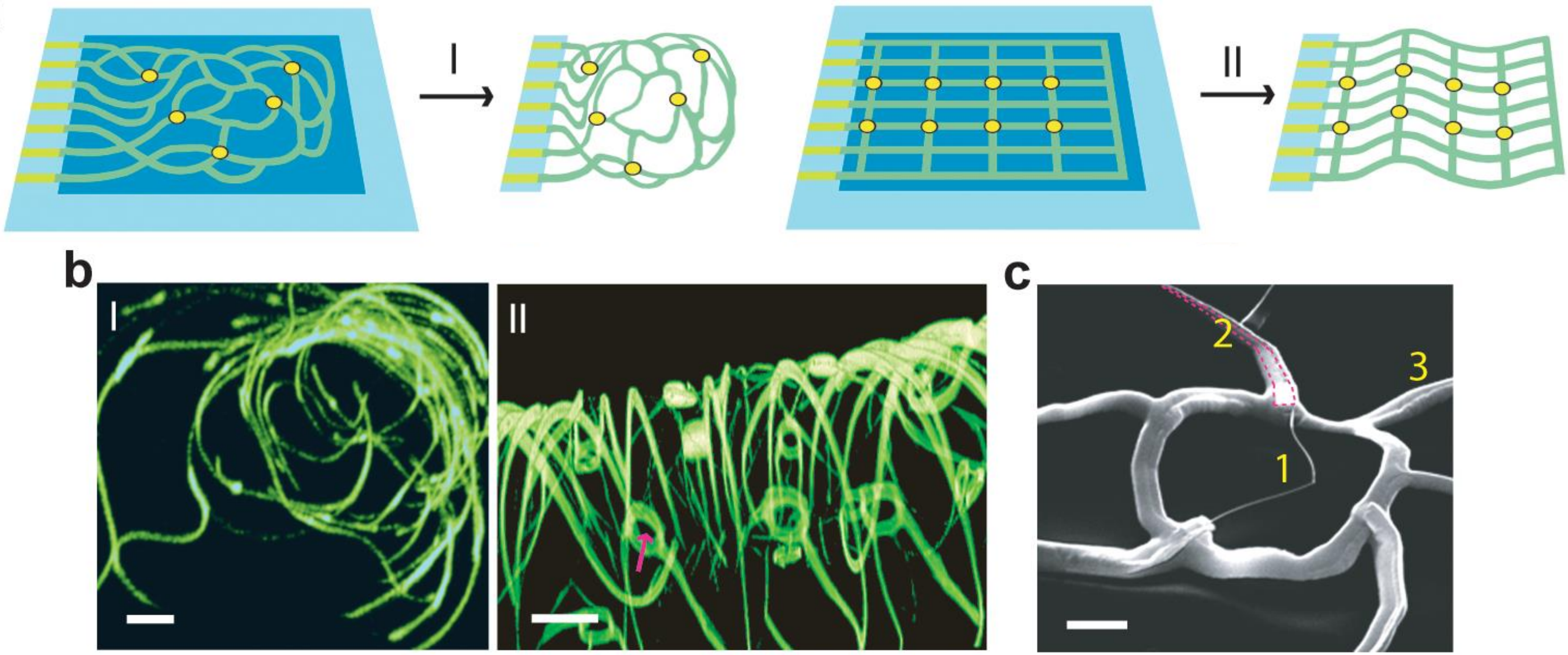


Macroporous 3D Nanoelectronics: Cyborg Tissue



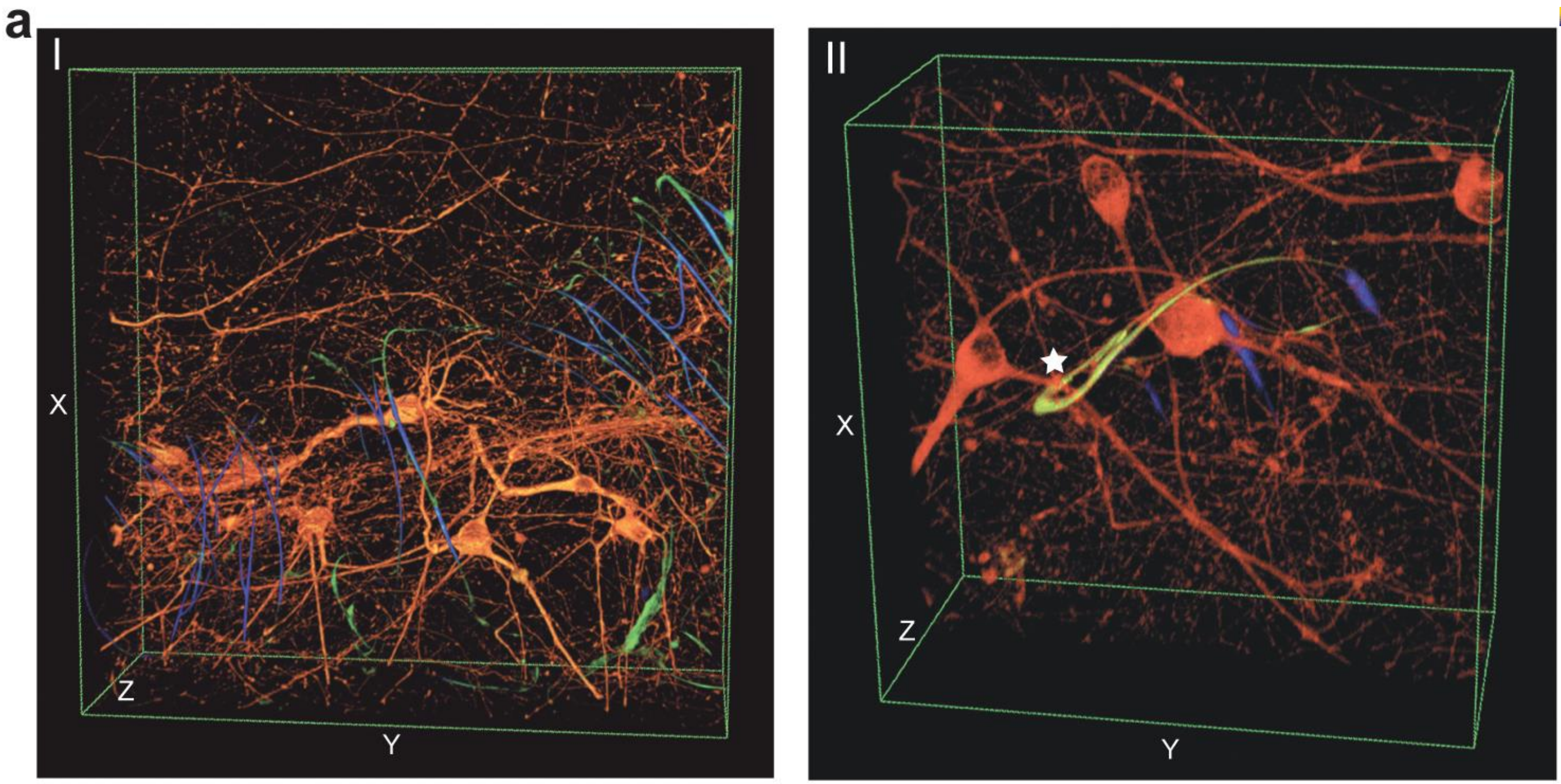
**** 3D addressable nanodevices ****

3D Macroporous Nanoelectronic Scaffolds



- 3D nanoelectronic scaffolds matrix prepared from 2D structures that are fully released from substrate.
- 3D scaffolds can exceed thickness >>1mm and maintain all key feature on micron-to-nanometer scale similar to natural biological scaffolds

‘Cyborg’ Neural Tissue



3D neural tissue ‘innervated’ with 3D nanoelectronic circuitry – future is only limited by our imagination!

Applied Neuroscience AFRL/RHCP

Neurobiological effects of direct current stimulation

Goal: provide protection and enhanced performance to the warfighter

Transcranial Direct Current Stimulation tDCS

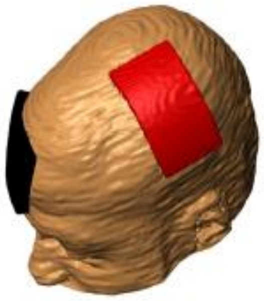
- Non-invasive, portable, well-tolerated neuromodulation.

- Low-intensity (1-2mA) current passed between scalp electrodes.

- Clinically used for: Depression, pain, migraine, epilepsy, PTSD, schizophrenia,tinnitus, rehabiliation, TBI, attention deficit, autism

- In laboratory setting used for: accelerated learning (reading, motor skills, threat detection), memory…etc.

QUESTION - Does a “simple” directed current modulate brain function? If so, how does it work, what does it change, what m are associated with the changes, are they repeatable, why do changes take place….



“Cellular Mechanisms of Transcranial Direct Current Stimulation”, PI - Marom Bikson, CUNY

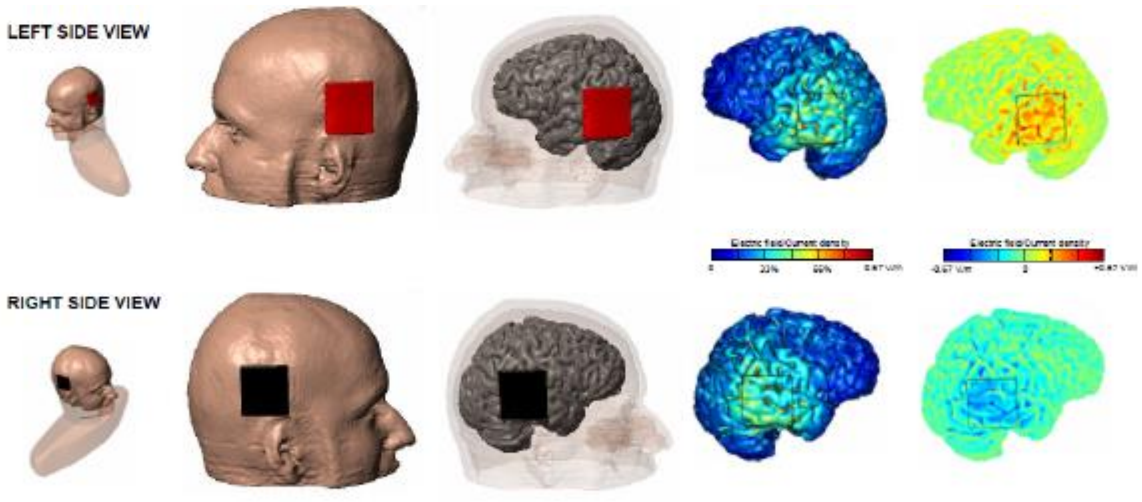
Transcranial DirectCurrent Stimulation

Two pad electrodes placed on head and connected to DC current stimulator.

Current passed between ANODE(+) and CATHODE(-)

DC CURRENT FLOW across cortex.

Current is INWARD under ANODE and OUTWARD under CATHODE



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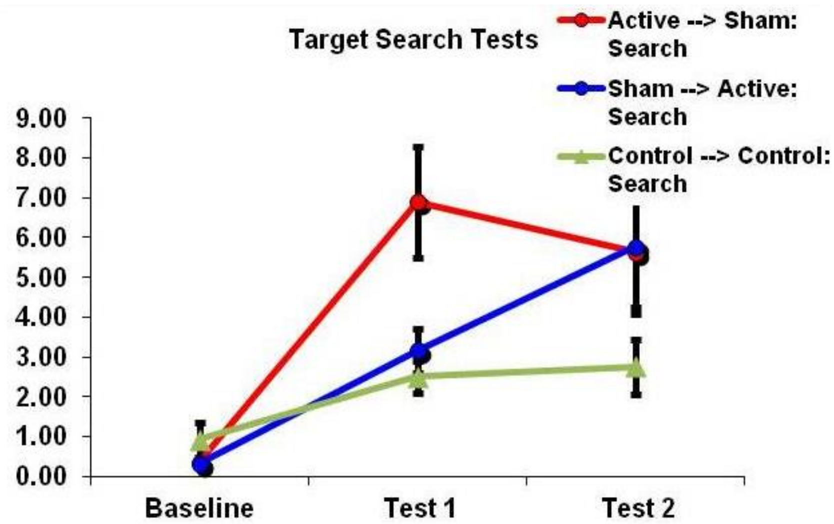
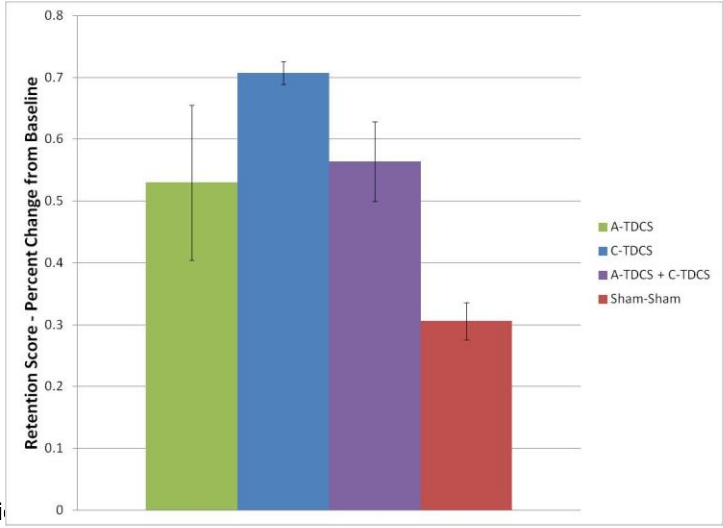
Introduction
tDCS

- Intervention/Treatment for neurological Disorders: Parkinson's, Psychiatric Disease & Stroke
- Cognitive improvements reported in both Disease and Control Populations
- Increased Cerebral Oxygen Saturation
- Improved Target Detection





Andy McKinley, PhD - AFRL

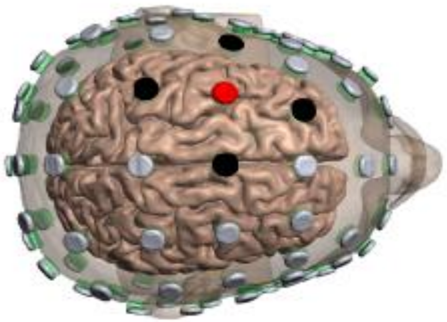
Hypothesis

Purpose of study: Identify biological pathways thought responsible for enhanced cognitive performance after tDCS

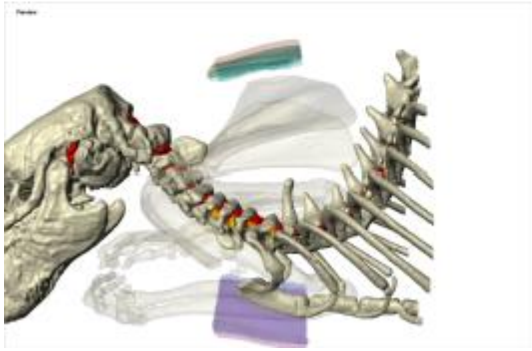
- **Objective 1: Identify pathways recruited by single bout of tDCS.**
- **Objective 2: Determine effects of repeated tDCS when coupled with training.**

tDCS Research at CUNY

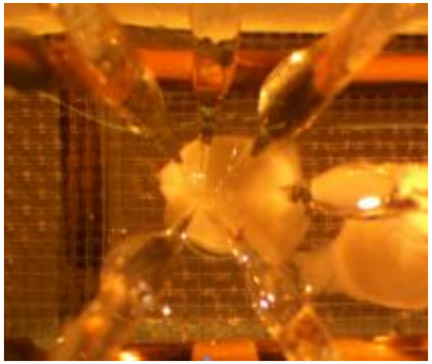
Computational Models



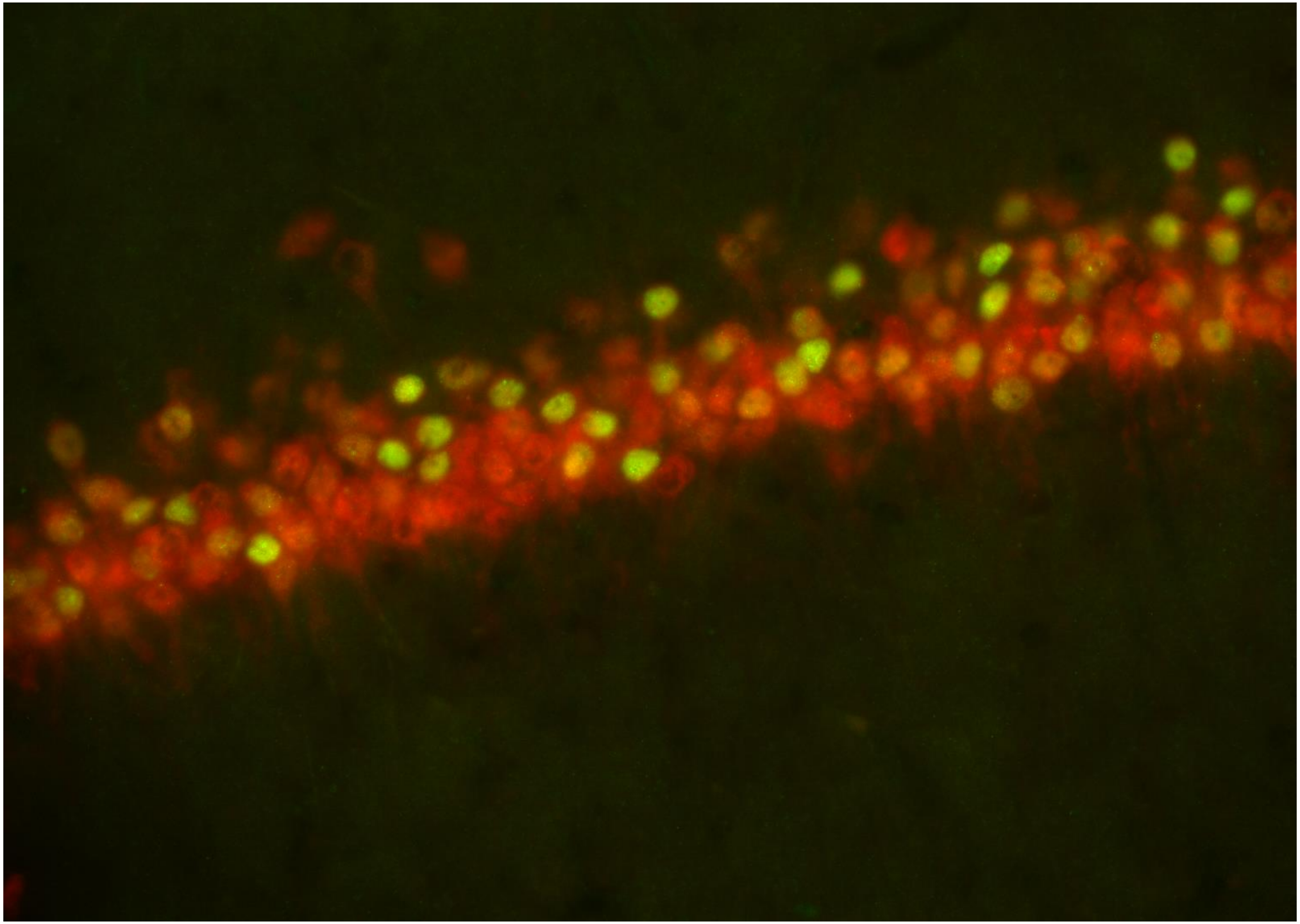
Animal DCS



Tissue/Brain Slice tDCS



Immunohistochemistry



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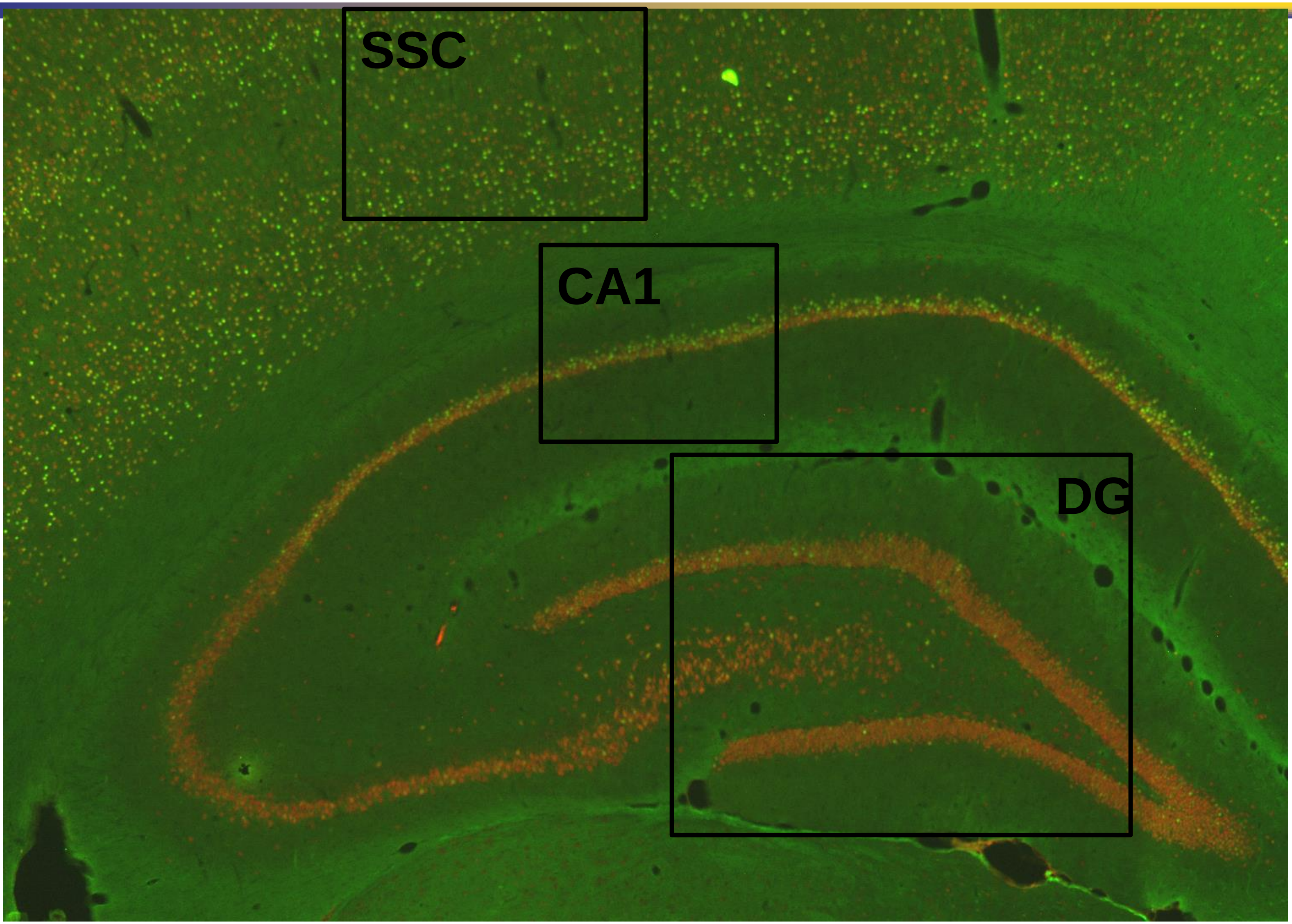
Immunohistochemistry



tDCS Summary

- Molecular, anatomical and genetic approach to studying changes associated with tDCS.
- Anecdotal evidence prevalent not much hard science to support claims
- 2 studies on going in Air Force Research Laboratory, one currently underway in academic setting looking at mechanisms.
- Potential benefit if positive results – decrease neurological fatigue, increased awareness, shortened learning time to task, focused attention

Biomarkers

- Interested in discovering new biomarkers from sweat, breath and odor associated with sweat and breath
- F22 grounding may have been prevented if O2 system was monitored and sensor development was available

  - Current new study looking at breath biomarker to determine early stage of hypoxia.
- Additional study for FY14 funding looking at the analytical identification of stress odors from human breath
- Potential benefit – if we can find a problem before it happens we can avoid costly mistakes

Summary

- Molecular, anatomical and genetic approach to studying microbe physiology and electron transfer.
- Microbial mechanisms led to communication capabilities and cyborg cell development idea
- Cyborg cell and 3D nanoelectric scaffold enables cellular communication from outside cell and ability to “program” individual cell as well as “correct”, change, direct cell to target.
- Transcranial Direct Current Stimulation studies are underway to determine the efficacy of this modality.